Surgical Anatomy of Parathyroid Glands with Emphasis on Parathyroidectomy

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Received April 26, 2006, Accepted May 17, 2006

Key words: Parathyroid gland – Parathyroidectomy – Clinical anatomy – Thymus

This work was supported by grants GA MZ ČR, projects No. 6856-3/2001 and 8308-5/2005.

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Abstract: Number, location and surrounding structures of parathyroid glands with emphasis on parathyroidectomy were studied on 101 cadaverous bodies. Number of collected samples from all known locations of parathyroid glands varied from three to five in one individual, with mean 3.71 ± 0.62. We identified 80% of samples as parathyroid glands. Mean number of correctly identified parathyroid glands in one individual was 2.77 ± 1.06. The rest 20% of collected samples were lymph nodes, fat particles and thyroid or lipothymic tissue.
Almost 30% more of inferior parathyroid glands were found in abnormal position in lipothymic tissue in comparison with their superior counterparts. We found several abnormities of vessels and cervical extensions of thymus. We also present case of brachiocephalic trunk, reaching the inferior pole of thyroid gland.
We recommend beginning of parathyroidectomy in circumscribed area 2 cm in diameter, 1 cm cranially to the intersection of the inferior thyroid artery and recurrent laryngeal nerve followed by preparation on dorsal surface of thyroid gland, along the course of inferior thyroid artery and recurrent laryngeal nerve, in cervical extensions of thymus and in paraoesophageal and retropharyngeal region. Success of parathyroidectomy is based on the knowledge and experience of surgeon.

Introduction

Parathyroid glands (PGs) are four small corpuscles localized on posterior aspect of the thyroid gland. They are about five millimetres in diameter, situated in fibrous tissue close to recurrent laryngeal nerve (RLN) and inferior thyroid artery (ITA) [1]. Superior PGs are usually dorsal to RLN, whereas inferior lies ventral to RLN [2]. This situation, anatomical norm, occurs in 80% of cases [2, 3]. In rest of cases, PGs vary in number, size, shape, color and above all in location (Table 1). About 80–90% of individuals have four PGs, 1–8% of individuals have three PGs and 2–9% of individuals have five PGs [3, 4]. In extreme cases there were found none or vice versa twelve PGs in one individual [3].

Location of PGs varies widely as a result of different degree of migration during embryonic development [5]. Thus, strange locations of PGs are not surprising [4, 6]. Bilateral symmetry is slightly higher in superior (80%), than inferior (70%) parathyroid glands [4].

Table 1 – List of possible ectopic localizations of parathyroid glands

Ectopic localization	Cervical extension of thymus
Intrathyroid	Thymus
Under capsule of thyroid gland	Parapharyngeal space
Close to ITA emerge	Paraoesophageal space
Thyrothymic ligament	Mediastinal fat

ITA – inferior thyroid artery

Parathyroid glands are known mainly for their role in homeostasis of calcium and phosphate metabolism. Hyperfunction of parathyroid glands is known as hyperparathyroidism [7, 8, 9]. Primary hyperparathyroidism, caused by adenoma (80%), hyperplasia (19%) or carcinoma (1%), is the most frequent cause of necessity of surgical intervention – parathyroidectomy (PTE) [4, 8, 9, 10, 11]. Parathyroidectomy is encumbered by list of the complicating factors [3, 8, 9, 12, 13], as listed in Table 2.

Accidental removal and/or damage of all PGs or their vascular pedicles during/after parathyroid or thyroid surgery result in permanent hypoparathyroidism – debilitating morbidity with permanent hypocalcaemia [3, 12]. One possibility of treatment of the permanent hypocalcaemia is still not feasible, but promising allotransplantation of PGs from cadaverous donors [14, 15, 16].

We undertook a comprehensive study of clinical anatomy of PGs to optimise the technique of parathyroidectomy. We focused on variability in number and location of PGs and surrounding structures with emphasis on cause of peroperative and postoperative complications.

Preliminary results of this study were published in abstract form [10, 11].

Materials and methods

This study was performed in collaboration of two anatomists, surgeon and pathologist on cadaverous bodies from the Institute of Anatomy and the Department of Pathology of the First Faculty of Medicine, Charles University, Prague. Together, 101 bodies (51 females and 50 males) at age 36 to 92 were dissected.

On neck, collar skin incision followed by midline incision and sternotomy was performed. Thorax was opened. Superficial neck fascia was cut in midline, infrahyoid muscles pulled laterally, lobes of the thyroid gland were detached from surrounding structures and pulled medially. Both RLN and ITA were cleaned. Close

Table 2 – List of complicating factors of parathyroidectomy and their consequences

Complicating factor	Result
Decreased number of PGs	Accidental removal of all PGs – hypocalcaemia
Ectopic localization of PG	Failure of PTE
Abnormal size of PG	Mismatch of PG with other tissue
Accidental injury of PGs	Hypocalcaemia, necessity of transplantation
Thyropathic field	Failure of PTE, injury of surrounding structures
Reoperation	Failure of PTE, injury of surrounding structures, scar
Injury of RLN	Vocal cord paralysis, voice hoarseness, breathing difficulty
Injury of ITA or abnormal vessel	Peroperative bleeding, postoperative hematoma

PG – parathyroid gland; PGs – parathyroid glands; RLN – recurrent laryngeal nerve; ITA – inferior thyroid artery; PTE – parathyroidectomy to the site of crossing of RLN and ITA, PGs were found. Preparation continued on the dorsal surface of thyroid gland, under the capsule of thyroid gland, along the course of RLN and ITA, in the cervical and mediastinal lipothymic tissue, in the anterior mediastinum and in the parapharyngeal and the paraoesophageal space.

The position, number and size of all samples were documented and analysed afterwards. Samples were removed, put in 4% paraformaldehyde, dehydrated by set of alcohols of ascending concentration, embedded to paraffin, cut to 10 μm section, stained with hematoxyline and eosin and analyzed by optic microscope.

Anatomical norm was defined as the presence of demanded PG within a circumscribed area 2 cm in diameter, 1 cm cranially to intersection of ITA and RLN, according to Bonjer and Bruining [3]. All abnormal anatomical relations of PGs and surrounding structures were dissected in detail and photographed. Fusion of superior and inferior PGs, also known as kissing pair, was distinguished from bilobular gland by the presence of a cleavage plane, according to Herrera and Gamboa-Dominguez [4].

Table 3 – Localization of left (sin.) and right (dx.) parathyroid glands

Localization	sin.	% of all sin.	dx.	% of all dx.	all	% of all
Superior parathyroid glands						
Anatomical norm	66	94.29%	65	92.86%	131	93.57%
Subcapsular	3	4.29%	3	4.29%	6	4.29%
Ipsilateral PGs fused	1	1.43%	1	1.43%	2	1.43%
Paraoesophageal	0	0.00%	1	1.43%	1	0.71%
Total	70	100.00%	70	100.00%	140	100.00%
Inferior parathyroid glands						
Anatomical norm	49	69.01%	44	63.77%	93	66.43%
Cervical extension	13	18.31%	15	21.74%	28	20.00%
Thyrothymic ligament	3	4.23%	5	7.25%	8	5.71%
Thymus	2	2.82%	2	2.90%	4	2.86%
Subcapsular	1	1.41%	1	1.45%	2	1.43%
Ipsilateral PGs fused	1	1.41%	1	1.45%	2	1.43%
Close to ITA emerge	1	1.41%	0	0.00%	1	0.71%
Total	71	100.00%	69	100.00%	140	100.00%

PGs – parathyroid glands; ITA – inferior thyroid artery

Table 4 – Success in identification of parathyroid glands

Tissue	No. of samples	% of total
Parathyroid	280	74.67%
Lymph nodes	40	10.67%
Fat tissue	28	7.47%
Thyroid gland	23	6.13%
Thymic tissue	4	1.07%
Total	375	100.00%

Dissection was performed on adult and mainly on old people, where thymic tissues are partially or completely replaced by fat. In our study, we are applying the term “lipothymic tissue” on thyrothymic ligament, cervical extensions of thymus and thymus according to anatomical position, not according to stage of lipomatous degeneration.

Numbers of collected samples and PGs were noted and statistically analysed as average numbers (mean ± S.E.M.).

Results

Together, 375 samples (100%) were collected from 101 bodies, 280 from them (74.67%) were identified as parathyroid glands (Table 4). We found 224 PGs in normal location – anatomical norm (Table 3, Figure 1A).

Number of parathyroid glands in one individual

Number of collected samples after dissection in all known locations of PGs varied from three to five in one individual, with mean 3.71 ± 0.62. Number of correctly identified parathyroid glands in one individual varied from one to four with mean number 2.77 ± 1.06. We did not found more than four parathyroid glands in any individual.

Size of collected PGs was in range of 4–8 mm. We found no significant correlation between age and size of PGs (data not shown). In spite of histological examination of all collected samples, we found no hyperplastic or tumorous PG in our study.

Inferior parathyroid glands have higher location variability

Superior PGs were found in anatomical norm in 93.57% of cases, in comparison with 66.43% of their inferior counterparts. Thus, incidence of abnormally located inferior PGs is 27% higher than in their superior counterparts (Table 3). This difference was probably caused by the occurrence of more than 28% of inferior PGs in different lipothymic tissues – cervical extensions, thyrothymic ligament and thymus (Table 3). No significant differences in location were seen between the same left and right PGs.

Majority of abnormal parathyroid glands were located in lipothymic tissues

Together, 28.57% of inferior PGs were located in lipothymic tissues, i.e. cervical extension of thymus, thyrothymic ligament and thymus (Table 3). This situation is presumably caused by a long and complex developmental pathway of PGs.

Other locations and positions of PG observed include subcapsular (5.72%), superior and inferior PGs fused together (2.86%), paraoesophageal (0.71%) and close to origin of ITA (0.71%).

No significant differences were observed between the same right and left PGs. In addition, total numbers of successfully identified right and left even so superior and inferior PGs showed no differences (Table 3).

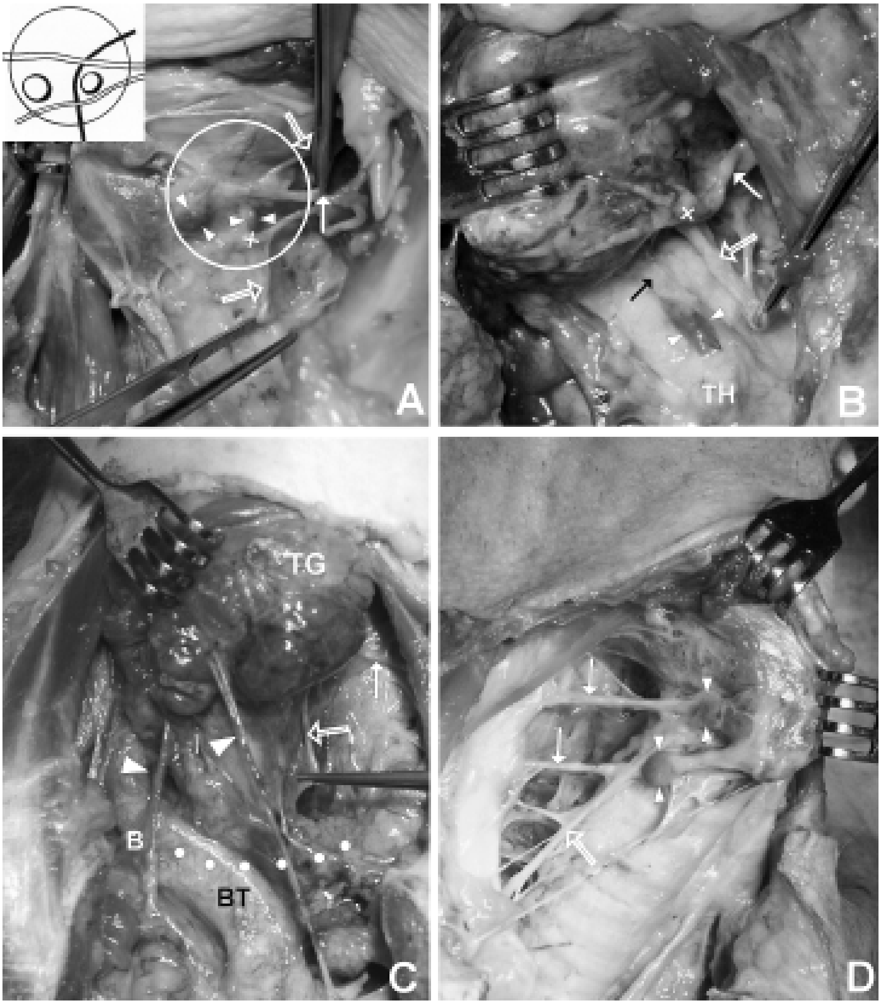

Figure 1 – Normal position of parathyroid glands (A) and three anatomical abnormities (B–D). A. Normal location of parathyroid glands (arrowheads) 1 cm above the intersection (marked as "x") of inferior thyroid artery (full arrow) and recurrent laryngeal nerve (empty arrows). Circle shows the most frequent location of parathyroid glands – anatomical norm. Left side view, thyroid gland pulled medially. Upper left corner – schematic drawing, showing parathyroid glands (circles) and the intersection of inferior thyroid artery (lower horizontal line) with recurrent laryngeal nerve (vertical). Upper horizontal line corresponds to inferior thyroid vein. B. Left inferior parathyroid gland (arrowheads), localized in cervical extension of thymus. Thyrothymic ligament also visible (black arrow). Empty arrow – recurrent laryngeal nerve. Full arrows – inferior thyroid artery. The intersection of recurrent laryngeal nerve and inferior thyroid artery marked as "x". Left side view, thyroid gland pulled medially. C. Higher branching (B) of the brachiocephalic trunk (BT) above the caudal pole of thyroid gland (TG, elevated). Left inferior thyroid artery – full arrow. Left recurrent laryngeal nerve – empty arrow. Inferior thyroid veins – arrowheads. Dotted line – superior border of the sternum. Anterior view. D. Doubled right inferior thyroid artery (full arrows). Arrowheads – parathyroid glands. Empty arrow – recurrent laryngeal nerve. Right side view, thyroid gland pulled medially.

Incorrectly identified parathyroid glands
Most frequent tissues mistaken for PG were brachiocephalic and paratracheal lymph nodes (10.67 %), fat tissue (7.47%), accessory nodule of thyroid gland (6.13%) and lipothymic tissue (1.07%) (Table 4).

Looking for superior right parathyroid glands, we incorrectly identified 21 samples (particularly for fat tissue – in 52.38%), looking for superior left PGs 25 samples (particularly for lymph node – in 48%), looking for inferior right PGs 25 samples (particularly for lymph node and thyroid tissue – each in 37.5%) and looking for inferior left PGs 24 samples (particularly for lymph node – in 48%). Thus, there was no predominant area for incorrect identification.

We found no correlation between age and success of identification of PGs (data not shown).

Anatomical variability of surrounding structures
During dissection of 101 bodies, we found several specific situations, which we recognized as possible sources of surgical complications during parathyroidectomy.

Anatomical variability of vessels
We found higher branching of the brachiocephalic trunk above the caudal pole of thyroid gland (Figure 1C), doubled inferior thyroid artery (Figure 1D) and both the right and the left ITA emerging from the right thyrocervical trunk – the right one running across and behind the posterior surface of thyroid gland to supply the left lobe of thyroid (not shown).

Anatomical variability of the lipothymic tissue
We found cervical extensions of thymus in almost all cases (95 of 101 bodies) and 20% of inferior PGs were found there (Table 3). They were localized mainly in the superior part of the cervical extensions of thymus (Figure 1B), but were also found in other parts along their whole course. Normally, cervical extensions of thymus run anterior to the left brachiocephalic vein (Figure 2A). We found situations, where the right extension runs anterior and the left one posterior to the left brachiocephalic vein (Figure 2B) or both cervical extensions were located posterior to the left brachiocephalic vein (Figure 2C).

Discussion
Our study shows higher variability of inferior than superior parathyroid glands, caused by their frequent location in lipothymic tissues. Few PGs were present under thyroid capsule, in paraoesophageal space, close to origin of ITA or fused with ipsilateral PG. If incorrectly identified, PGs were mistaken particularly for lymph nodes, fat and thyroid tissue.

Anatomical norm
We found 80% of PGs in circumscribed area 2 cm in diameter, 1 cm cranially to the intersection of ITA and RLN – in an anatomical norm [3]. Superior PGs were

usually posterior to the RLN, whereas their inferior counterparts anterior to the RLN, similar to data reported by Pyrtek and Painter [2].

The rest 20% of cases can significantly complicate parathyroidectomy. These cases might prolong surgery with requirement of enlargement of the incision and the operative field. Rarely, the sternotomy, resulting in cosmetically unfavourable scar, might be also necessary [3]. Worst, demanded PG is not found and/or important anatomical structure such as important vessel or recurrent laryngeal nerve is damaged, resulting in preoperative bleeding, postoperative hematoma and/or vocal cord paralysis [3, 12, 13]. Thus, all possible locations of PGs should be considered before the onset of surgery.

Parathyroid glands in lipothymic tissue

According to our results, almost 29% of inferior PGs were localized in different thymic tissues. Unfortunately, majority of these PGs were localized in cervical extensions of thymus and thymus, localized under the level of cranial border of sternum (Figure 2A–C), whereas only 6% of them were localized in thyrothymic ligament, close to thyroid gland.

Thus, almost 23% of the inferior PGs are not accessible by standard collar incision. This disadvantage is usually corrected by the backward bending of the

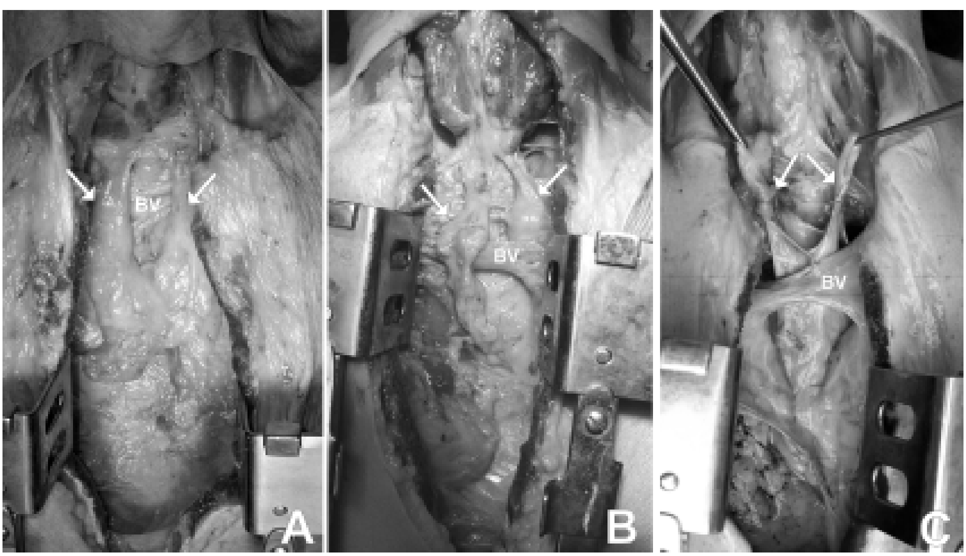

Figure 2 – Normal position of cervical extensions of thymus (A), in correlation with two abnormities (B, C). A. Normal position of cervical extensions of thymus (arrows), which are anterior to left brachiocephalic vein (BV). B. Right cervical extension (left arrow) located anterior to left brachiocephalic vein (BV), left cervical extension (right arrow) is posterior to left brachiocephalic vein. C. Both cervical extensions (arrows) located posterior to left brachiocephalic vein (BV).

head, but sometimes partial or total sternotomy must be performed, after the exclusion of location of demanded PG in cervical region. If location of abnormal PG is known previously due to different imaging methods, such as ultrasonography, computed tomography, magnetic resonance imaging or 99mTc-sestamibi scan [17], miniinvasive treatment without sternotomy is also possible [18]. Alternatively, minimal incision PTE without preoperative imaging methods is also possible [19]. But, preoperative imaging methods can lead to false positive results [20], so the surgical exploration based on precise anatomical knowledge still remains the principal method of localizing abnormal PGs in primary hyperparathyroidism.

Incorrectly identified parathyroid glands

We identified almost 75% of collected samples as PGs. Surprisingly we observed no difference in success of identification between superior and inferior PGs or between PGs of right and left side. This fact indicates there is no predominant region for incorrect identification of PGs. On the other hand, these data support conviction of experience of surgeon as a limit of proper identification of PGs. Throughout our study we similarly observed increasing success in identification of PGs between sampled tissues (data not shown).

During PTE, demanded PGs are usually found spherical and enlarged due to hyperfunction. In addition, they have different colour than other structures and the surgeon is usually guided by results of the preoperative imaging methods [3]. We found no hyperplastic or tumorous PG in our study.

Parathyroid glands were mismatched particularly for lymph nodes (Table 4), probably due to their similar colour and/or variable size and location. Incorrect identification of lymph node as PG also occurs during surgical removal of adenoma, which has similar scirrhous consistence [3]. Factors of proper identification of lymph nodes cited include their more rounded configuration and adherence to surrounding tissues [4]. Fat lobule and accessory nodule of thyroid gland can also be accidentally removed instead of PGs. Fat lobules are but more friable and do not have PG consistency or lace of work of blood vessels on surface. Thyroid nodules are always harder, connected with thyroid gland, more reddish and less homogenous than PGs [3, 4].

In case of unknown localization of the demanded parathyroid gland, it is advisable to perform a radioguided parathyroidectomy based on the injection of 99mTc-sestamibi [21].

Regional anatomical variability and complications of PTE

Several anatomical varieties have been described. We found two different cases of an aberrant vessel, but many others are possible [1]. Atypical branching of vessels (Figure 1C, D) can cause intraoperative bleeding and/or postoperative hematoma [3, 12, 13]. Damage of ITA can lead to ischemia of all ipsilateral PGs.

Peroperative injury of atypically branching brachiocephalic trunk can cause fatal bleeding, as described by Buist and Barnes [22]. Thus, all regional vessels should be considered during parathyroidectomy or other surgeries of PGs.

We did not found any case of abnormal course of the RLN. However, contusion and/or neurotmesis of the RLN, resulting in a vocal cord paralysis, are usually estimated as the most important complicating factor of the parathyroid surgery [12, 13]. Thus, we fully support the idea of peroperative observation and electromyographic monitoring of the RLN [3, 13, 23].

Variability in location of cervical extensions of thymus [Figure 1B, 2B–C] can also cause unintentional damage of vessels, the left brachiocephalic vein in particular. More frequent is but a decreased chance of finding the PGs in presumed location, resulting in necessity of enlargement of the surgical field and sometimes also a sternotomy [3].

Collection of parathyroid glands from cadaverous donors

Occurrence of the worst complication of parathyroid surgery, i.e. complete loss of PGs in parathyroid and thyroid surgeries is fully depending on surgeon's skills, experience and knowledge of parathyroid anatomy [3, 13].

Hyperplasia of parathyroid glands is usually solved by subtotal parathyroidectomy with the preservation of the rest parathyroid tissue marked with clip for subsequent identification of spared parathyroid tissue in future, if necessary. In parathyroid hyperplasia, complete loss of parathormone secretion can be prevented by cryopreservation of hyperplastic PGs, with contingency of a subsequent autotransplantation of PGs into forearm muscle in case of failure of the PTE [14].

If all PGs are removed during thyroid surgery, complemented by intraoperative monitoring of the parathormone, immediate replantation of PGs into forearm muscle is also possible. In other cases, the only way to prevent lifelong supplementation with calcium and analogues of vitamin D, together with prevention of complications of chronic hypocalcaemia is allotransplantation of parathyroid cells from cadaverous donors [16], unfortunately still not developed for the use in clinical practice. But, study by Lee et al. [15] reveals promising results by microencapsulation of parathyroid tissue to a specialized semipermeable membrane to protect it from rejection.

Recommended course of parathyroidectomy

We recommend beginning of the PTE in previously described circumscribed area 2 cm in diameter, 1 cm cranially to the intersection of ITA and RLN. If parathyroid glands are not found, continue preparation on dorsal surface of thyroid gland, along the course of ITA and RLN, in cervical extensions of thymus and in paraoesophageal and retropharyngeal region. Make sure you know where RLN and ITA and their branches occur during the whole PTE.

Conclusions

Based on this study and our previous reports [8, 9, 10, 11], we fully recommend (i) training of surgeon on cadaverous bodies to gain knowledge and experiences about anatomical variability of PGs and surrounding structures, (ii) the use of preoperative and peroperative imaging methods and (iii) the surgical exploration of "anatomical norm" region to prevent damage of important structures and/or removal of incorrect PG or even all PGs.

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